

The present application is related to U.S. Application No. 09/445,653. Both applications are directed to compositions for delivery of biological agents comprising *inter alia*, a supramolecular complex including as constituents a block co-polymer having at least one nonionic, water soluble segment and at least one polyionic segment, and at least one charged surfactant having hydrophobic groups, with the charge of the polyionic segment of the block co-polymer being opposite to the charge of the surfactant.

A final rejection was entered in this application and in the '653 application, in which all of the claims were found to be obvious under 35 U.S.C. §103 in view of the combined disclosures of Hubbel et al. (U.S. Patent No. 5,410,016), Ahmad et al. (U.S. Patent No. 5,112,611), Nakayama et al. (U.S. Patent No. 5,531,917) and Weiner et al. (U.S. Patent No. 5,171,737).

In a telephone interview between the undersigned and Supervisory Primary Examiner Padmanabhan on January 22, 2003, it was agreed that the §103 rejection outstanding in the '653 application would be overcome by amending the claims to include a recitation to the effect that the block copolymer constituent of the claimed composition is not cross-linked. It was recognized by Supervisory Primary Examiner Padmanabhan that such an amendment is consistent with the arguments for patentability advanced by applicants during the course of prosecution of these applications.

In accordance with the amendment submitted herewith,

claim 1 of the present application has been amended by the additional recitation that the "block copolymer constituents are not cross-linked to form networks". This amendment is in keeping with the agreement reached between the undersigned and Supervisory Primary Examiner Padmanabhan, as noted above, and finds support in the present specification, page 6, line 3 through page 7, line 15. As a result of this amendment, it is believed that the claimed invention is clearly distinguishable over the combined disclosures of Hubbel et al., Ahmad, Nakayama et al. and Weiner. In this regard, it is noted that the photopolymerizable, biodegradable hydrogels of Hubbel et al. are adapted to be cross-linked so as to form networks. See Column 5, lines 15-64 and Column 8, lines 5-27 of Hubbel et al.

Applicants wish to take this opportunity to dispute once again the Examiner's assertion that the disclosures of Hubbel et al., Ahmad et al., Nakayama et al. and Weiner et al., in and of themselves, provide the motivation required for one of ordinary skill in the art to arrive at applicants' invention.

Although Nakayama et al. may reasonably be viewed as providing a solution to the purported problem of Biopraxe instability in contact lens cleaning compositions, it does not reasonably provide any suggestion or motivation for those skilled in the art to similarly attempt to stabilize papain, in the event that papain were incorporated in the biodegradable hydrogels of Hubbel et al., as proposed by the Examiner. The data provided in Nakayama et al. pertain exclusively to the stabilizing effect

of certain surfactants on Biopraxe in a contact lens cleaning composition. Biopraxe is a proteolytic enzyme derived from a microorganism of the genus Bacillus. See Column 3, lines 20-25 of Nakayama et al. There is no data set forth in Nakayama et al. that tends to show that papain would exhibit similar instability in a contact lens cleaning composition. Indeed, as noted in the attached page from the SERVA Electrophoresis GmbH web site, papain is "known for its unusually high stability" and "as crystalline suspension in NaCl solution at near neutral pH, papain can be stored for many months at 4°C without any significant loss of activity". The conditions under which papain exhibits such stability are comparable to the conditions specified in Table 1 of Nakayama et al.

In any event, maintaining proteolytic enzyme stability is certainly not regarded as a problem in the case of the biodegradable hydrogels of Hubbel et al., with which papain is proposed to be combined. It is noteworthy in this connection that Hubbel et al., at Column 16, lines 50-52 disclose that the water present in the hydrogels described therein "can be expected to help proteins and enzymes entrapped in such gels in maintaining their native conformation and reducing deactivation". Thus, rather than promoting enzyme instability, the water content of their hydrogels is considered by Hubbel et al. as beneficial for maintaining enzyme conformation and reducing deactivation. This is not merely theoretical conjecture by Hubbel et al. On the contrary, the compatibility between proteolytic enzymes and

the hydrogels of Hubbel et al. was demonstrated in practice. As stated at Column 21, lines 33 and 34 of Hubbel et al., "[f]ully active tPA can be released for periods up to at least two (2) months.

In summary, there is plainly no motivation provided in the disclosures of Hubbel et al., Ahmad et al., Nakayama et al. and Weiner et al. for combining them in the manner proposed by the Examiner, and even if combined, the claims presented herewith are clearly patentably distinguishable over the resulting combination.

Accompanying this submission is an Information Disclosure Statement listing references which the Examiner is respectfully requested to consider and make of record in this application.

In view of the present submission, all of the claims now pending in this application are believed to be in condition for allowance. Accordingly, the issuance of a Notice of Allowance is in order, and such action is earnestly solicited.

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Enclosure: Papain (from SERVA Electrophoresis GmbH
web site - 2 pages)

MARKED-UP VERSION OF THE AMENDED CLAIM

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1. (Amended) A composition of matter comprising a supramolecular complex comprising as constituents a block copolymer, having at least one nonionic, water soluble segment and at least one polyionic segment, and at least one charged surfactant having hydrophobic groups, the charge of said surfactant being opposite to the charge of the polyionic segment of said block copolymer, wherein the block copolymer constituent is not crosslinked to form networks, the constituents of said complex [being] are bound by interaction between said opposite charges and between surfactant hydrophobic groups, and with the proviso that when said complex comprises an anionic surfactant having a biological activity, said anionic surfactant has a net charge of no more than about 10.